

Claims

1. A method for the treatment of soft tissue disease in a mammalian subject, said method comprising administering to said subject a therapeutically effective quantity of a soft tissue targeting complex of thorium-227 and a complexing agent, wherein said quantity is such that an acceptably non-myelotoxic quantity of radium-223 is generated *in vivo* by nuclear decay of the administered thorium-227.
2. A method as claimed in claim 1 wherein said subject is human or canine.
3. A method as claimed in claim 1 or claim 2 wherein said therapeutically effective quantity is at least 18 kBq of thorium-227 per kilogram bodyweight.
4. A method as claimed in any one of claims 1 to 3 wherein said therapeutically effective quantity is at least 75 kBq of thorium-227 per kilogram bodyweight.
5. A method as claimed in any of claims 1 to 4 wherein said acceptably non-myelotoxic quantity is less than 300 kBq radium-223 per kilogram bodyweight.
6. A method as claimed in claim 5 wherein said acceptably non-myelotoxic is less than 150 kBq of radium-223 per kilogram bodyweight.
7. A method as claimed in any of claims 1 to 6 wherein said complex comprises chelated thorium-227 linked to a ligand selected from the group of antibodies,

antibody constructs, antibody fragments, constructs of antibody fragments and mixtures thereof.

8. A method as claimed in any of claims 1 to 7 wherein said soft tissue disease is a malignant disease.
9. A method as claimed in claim 8 wherein the malignant disease is a disease selected from the group of carcinomas, sarcomas, myelomas, leukemias, lymphomas and mixed type cancers.
10. A method as claimed in any of claims 1 to 9 wherein said subject is also treated to combat the myelotoxicity of the radium-223 generated therein.
11. A method as claimed in claim 10 wherein said subject is provided with stem cell treatment.
12. A method for the treatment of soft tissue disease in a mammalian subject, said method comprising administering to said subject a therapeutically effective quantity of a soft tissue targeting complex of thorium-227 and a complexing agent, wherein said quantity is D_{add} as calculated from formula I below, such that an acceptably non-myelotoxic quantity D_{Ra} of radium-223 is generated *in vivo* by nuclear decay of the administered thorium-227;

$$D_{add} = \frac{D_{Ra} \times T_{Th} \left((T_{Bio})^{-1} + (T_{Th})^{-1} \right)}{1.65} \quad (I)$$

wherein:

T_{Bio} is the biological half-life of said soft tissue targeting complex of thorium-227

and a complexing agent;

T_{Th} is the physical half-life of ^{227}Th (18.7 days);

D_{add} is the activity of the administered ^{227}Th complex (kBq/kg); and

D_{Ra} is the acceptably non-myelotoxic amount of ^{223}Ra .

13. A method as claimed in claim 12 wherein D_{Ra} is 200 kBq/kg

14. A method as claimed in any of claims 1 to 13 in combination with at least one further treatment modality selected from surgery, external beam radiation therapy, chemotherapy, endoradionuclide therapy with radionuclides other than ^{227}Th , and/or tissue temperature adjustment.

15. A pharmaceutical composition comprising a soft tissue targeting complex of thorium-227 and a complexing agent, together with at least one pharmaceutical carrier or excipient.

16. A soft tissue targeting complex of thorium-227 and a complexing agent.

17. A complex as claimed in claim 16 wherein thorium-227 is chelated by a derivative of 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid.

18. A method for forming a complex as claimed in claim 17 comprising heating said thorium-227 with said derivative of 1,4,7,10-tetraazacyclododecane-1,4,7,10-

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tetraacetic acid to form a chelated thorium-227 and subsequently attaching said chelated thorium-227 to a targeting moiety.

19. A kit for use in a method as claimed in any of claims 1 to 14, said kit comprising a solution of a soft tissue targeting complex of thorium-227 and a complexing agent together with instructions for the use of said solution in said method.

20. A kit for use in a method as claimed in any of claims 1 to 14, said kit comprising a complexing agent capable of complexing thorium ions; where said complexing agent is not a soft tissue targeting complexing agent, a soft tissue targeting compound, optionally together with a linker compound, conjugatable to said complexing agent to yield a soft tissue targeting complexing agent; and instructions for the preparation therefrom of a soft tissue targeting complex of thorium-227 and a complexing agent, and optionally also for the use of said complex in said method.